Florida Department of Health
Division of Medical Quality Assurance

Pharmaceutical Pedigree

Ensuring Product Quality & Standards

Board of Pharmacy / Drugs, Devices, and Cosmetics
Gregg Jones, R.Ph.

NABP / AACP District III Meeting
Orlando, FL - August 5, 2007

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Presentation Outline

1. Pedigree History Review
2. Overview Federal Pedigree Rule and Status
3. Florida Pedigree requirements for Drug Wholesalers and Pharmacists
4. Safety of Prescription Drug Supply and Pedigree.
5. Issues and Challenges

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Presentation Outline

- This discussion will not cover
  - Internet sales without a prescription
  - Internet sales with a medical questionnaire
  - Diversion of Controlled Substances
  - Importation of Drugs from Canada, EU
- This is about efforts to prevent Adulteration of the Drugs that are crucial to delivery of healthcare.

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Concepts and Terms

- 3PLs – Third Party Logistic Companies
- Rx Drugs in Medical Device Trays/Kits
- Distribution of INDs – Phase 4 post approval
- Virtual Manufacturers
- Contraband
- Point of Distribution vs Point of title passage
- Pharmaceutical Brokering
- Wholesale Distribution by Pharmacies
- Authentication of Pedigrees
- Wholesale Distribution of APIs
- RFID
- Serialization

Drug Wholesaler Oversight

- As with the practice of Pharmacy, left to the States
- States license wholesalers under the Boards of Pharmacy, Departments of Health, Agriculture, Education, and Secretary of State
- State Variations
  - Many states do not inspect drug wholesalers
  - Do not prohibit licensing homes
  - Felons can get permits
- 50 different regulations – modeled after FDA Rule

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U.S. DRUG LAW –

SAFETY and EFFECTIVENESS

1906 – Food and Drug Act: Strength and Purity

1938 – Federal Food, Drug and Cosmetic Act – Manufacturer Proven Safety

1951 – Durham Humphrey Amendments - Rx Requirement for Physician Supervision

1962 – Kefauver – Harris Amendments– Proven Effectiveness

1987 - Prescription Drug Marketing Act

THE AMERICAN PHARMACEUTICAL ASSOCIATION

1852 – At the Philadelphia College of Pharmacy due to a need for standards of education and quality control of imported drugs

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U.S. Prescription Drug Business Facts

- 2002 - 3,340,000,000 outpatient prescriptions [1]
- U.S. drug sales 2006 - $274.9 billion [2]
  - #1 Lipitor $7,691,000,000
  - #5 Procrit $3,192,000,000
  - #7 Epogen $2,990,000,000
- 3 Major National Drug Wholesalers
  - McKesson - $83 Billion Rx 2006 [3]
  - Cardinal - $70 Billion Rx 2006 [3]
  - AmerisourceBergen - $56 Billion Rx 2006 [3]

1. NDCHealth, a healthcare information services company. Atlanta, GA, 4/1/2003 www.ndchealth.com.
2. Http://www.imshealth.com/ims/portal/front/articleC/0,2777,6599_3665_80415465,00.html
3. Annual Reports

Large Wholesale Distribution Center

- **Typical Center**
  - **Square Footage 200,000 +**
  - **Inventory Value >$250 Million**
  - **SKUs 42,000**
  - **Employees 250**
  - **Customers 1,500**
  - **Geographic Coverage – Often Several States**
- **Statistics (Daily)**
  - **Pieces Picked 110,000**
  - **Totes and Cases Delivered 13,000**
  - **Customer Stops ~ 1,500**

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Pedigree History (PDMA)

- The PDMA (1987 Prescription Drug Marketing Act) became law on April 22, 1988
- Result of FBI Operation "Pharmony" and state investigations (CA, FL,GA, and OH)
- Congress decided there were insufficient safeguards in the prescription drug distribution system to prevent the introduction of substandard, ineffective, or counterfeit drugs and that a wholesale drug diversion submarket had developed that prevented effective control over, or even routine knowledge of, **the true sources of drugs**.

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Pedigree History – Operation "Pharmony"

- Millions of Dollars of Rx Drugs - U.S. Goods Returned Stop Saled in Florida. Opened Door for Counterfeit Drugs
  - Demulen – Birth Control Pill
  - Ceclor – Oral Antibiotic
  - Injectable Pipercil – Injectable vials
- Special Priced Hospital Drugs diverted to Wholesalers
- Sample Rx Drugs diverted to Pharmacies
- Wholesalers in 50% of States Not Licensed
- 66 Persons tendered guilty pleas. Corporate officers, physicians, pharmacists, sales reps.

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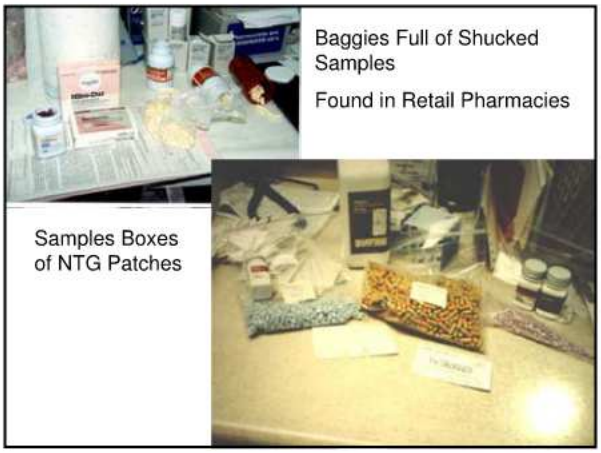
J3 JonesMG, 1/29/2007


Baggies Full of Shucked Samples
Found in Retail Pharmacies
Samples Boxes of NTG Patches

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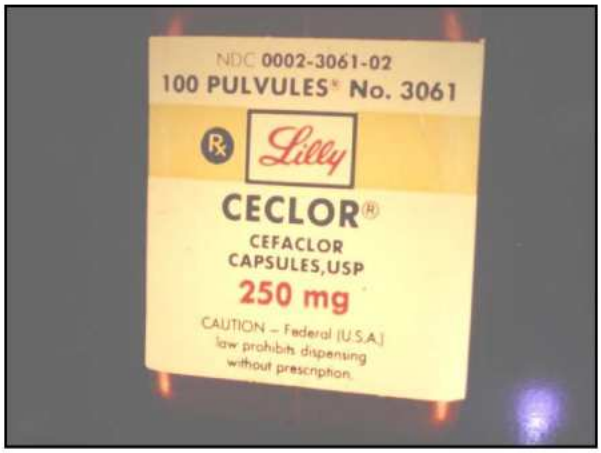

Counterfeit Ceclor - USGR

GALAXY INTERNATIONAL
6-G, 3-6, MINGEN ROW,
KOWLOON, HONG KONG.

DATE: 16.May.85
INVOICE No: 6016
SALE NOTE No:
INDENT No:

INVOICE of 1 (One) Carton Case of Health Aids Shipped in good order and condition by Messrs GALAXY INTERNATIONAL per Flying Tiger,
sailing on/about 18.May.85 from Singapore to Boston,
on account and risk of Messrs natali Inc, P.O.Box 561703 Miami, Florida 33156 U.S.A
Terms C.O.D
Mark
Insurance covered with by buyers.

Marks and Numbers	Quantity	Description	Price U.S.$	Amount U.S.$
1				
	848 pcs	Ceclor 250 mg.	63.00	53,424.0
	320 pcs	Ceclor 500 mg.	120.00	38,400.0
		Total F.O.B Singapore	US.$	91,824.0

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Federal Pedigree

21 USC 353(e)(2)(A)

- Each person who is engaged in the wholesale distribution of Rx drugs and who is not the manufacturer or authorized distributor of record, shall, prior to each wholesale distribution of such drug, provide a statement to the person who receives the drug identifying each prior sale, purchase or trade of such drug.

Federal Pedigree

- **Pedigree Requirements Apply to:**
  - Human Prescription Drugs (Even if sold to Vets)
  - Medical Device Kits/Trays with Rx Drugs
  - APIs - Active Pharmaceutical Ingredients (Bulk Drug Substances)
- **Pedigree Requirements Do <u>Not</u> Apply to:**
  - Veterinary prescription drugs
  - Drug samples

Federal Pedigree

- 21 USC 353(e)(3)(A) Authorized distributor - a distributor with whom a manufacturer has established an ongoing relationship.
- 1999 final rule
  - 21 CFR 203.3 Ongoing relationship - includes a written agreement between manufacturer and wholesaler
  - 21 CFR 203.50 Pedigree information traceable back to first sale by manufacturer

Pedigree History (PDMA) Review

- Problem areas:
  - Sample Rx Drug Diversion
  - Re-importation of Exported Rx Drugs
  - Diversion of Hospital Priced Rx Drugs
  - Unlicensed Rx Wholesale Distributors
- PDMA of 1987 - Solutions
  - Prohibits Rx Drug Re-importation
  - Prohibits Wholesale of Rx Drugs sold to Health Care Entities
  - Prohibits sale of Rx Samples and Increased Accountability
  - Requires Rx Drug Wholesalers to be licensed in accordance with FDA rules (21CFR)
  - Requires Rx Drug Pedigree - **Weakness ADR**

Authorized Distributor of Record

Authorized Distributor of Record =

Florida Law Section 499.0121 (6)(d)

Authorized Distributor of Record

Expired 7/1/2006

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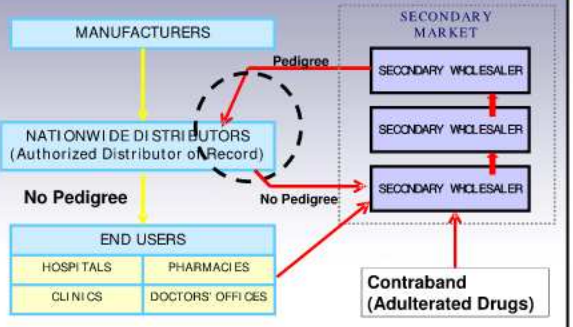
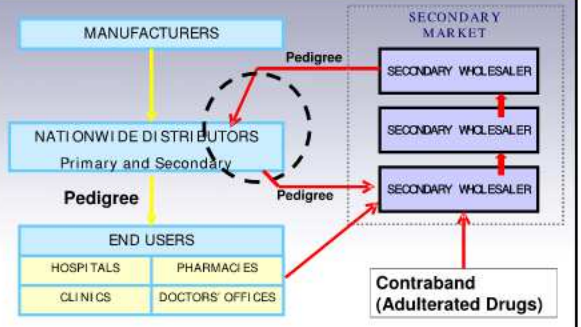
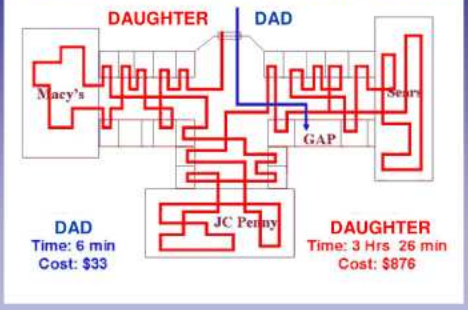
DRUG DISTRIBUTION With ADR



DRUG DISTRIBUTION Without ADR



Mission: Go to Gap, Buy a Pair of Pants



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Federal Pedigree

FDA responsible for rules implementing PDMA

- 3/14/1994 - FDA proposed rule on PDMA including pedigree provision
- 12/4/1999 - FDA issued final regulations
  - Information required on pedigree including lot number
  - Pedigree required back to Manufacturer
- 6/14/2006 - FDA announced effective date of 12/1/06
- 9/20/2006 - Secondary wholesalers filed in Federal District Court.

Robert Drucker, RxUSA Wholesale
The National Coalition of Pharmaceutical Distributors

- 11/13/2006 – FDA CPG on Pedigree

Federal Pedigree

- 11/22/2006 – Wholesalers asked for Preliminary injunction to stay effective date of rule
- 12/8/2006 – Preliminary Injunctions against FDA issued by Federal District Court of Eastern NY
  - Enjoins requirement of pedigree back to Mfr. By NADR
  - Enjoins requirement of certain info on pedigree, including lot #, and container size.
- 4/19/2007 – FDA appeals December 2006 Injunction
  - FDA'S claims that congressional intent requiring pedigree back to manufacturer is clear in PMDA.

Federal Pedigree

Current FDA Position on Pedigree

- As long as the court's order is in effect, FDA does not intend to initiate any enforcement actions against any wholesalers solely for:
  - failing to include lot numbers, dosage, container size, or number of containers on a pedigree; or
  - failing to provide a pedigree that goes back to the manufacturer so long as the pedigree otherwise identifies the last authorized distributor of record that handled the drugs.

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Florida Pedigree History
Major Events

2001

- Large increase in number of wholesalers and increase in counterfeits

2002

- Department of Health Ad Hoc Pedigree Committee studied Pedigree and Drug Wholesale regulations for 10 months.

2003

- Statewide Grand Jury investigated the Drug Wholesale Industry - Issued Report Feb '03
- Office of Program Policy Analysis and Governmental Accountability (OPPAGA) studied the regulation of Drug Wholesale Industry – Issued Report Feb '03
- Florida SB 2312 – Prescription Drug Protection Act May '03
- Congressional Hearing – June '06

Florida Pedigree History
Major Events

2006

- Effective 7/1/2006 - Florida Law required a full pedigree for every bottle of every drug distributed by wholesaler
- HB 371 – Created Direct Purchase Pedigree Alternative; Passed the last minute of the last hour of the last day of the 2006 Legislative Session.

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"The intent of the pedigree paper law is to protect the public by safeguarding our drug supply;"

FIRST INTERIM REPORT OF THE SEVENTEENTH STATEWIDE GRAND JURY - February 2003

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oppaga
OFFICE OF PROGRAM POLICY ANALYSIS & GOVERNMENT ACCOUNTABILITY

October 2005 Report No. 05-49

The Florida Legislature - OPPGA

Wholesaler compliance with pedigree paper requirements is vital to ensuring the safety and integrity of Florida's wholesale prescription drug market.

Progress Report: Legislature Strengthens Pedigree Paper, Wholesaler Permit Requirements to Better Ensure Safe Prescription Drugs, **Report No. 05-49, October 2005**

DRUG DISTRIBUTION

MANUFACTURERS

NATIONWIDE DISTRIBUTORS

END USERS

HOSPITALS	PHARMACIES
CLINICS	DOCTORS' OFFICES

GOAL:

CLOSED DRUG DISTRIBUTION SYSTEM FROM THE MANUFACTURER TO THE PATIENT

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Drug Distribution Models

1. Manufacturer → Retailer
2. Manufacturer → Wholesaler → Retailer
   Repackager
3. Manufacturer → Wholesaler → Wholesaler → Retailer
   Repackager

Other Source of Drugs
(e.g., institutional pharmacies, closed door pharmacies, foreign markets

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THE SECONDARY (GRAY OR DIVERSION) MARKET

Counterfeit Drugs

Special reduced price drugs from Closed Pharmacies, Hospitals, Physicians

Drugs intended for export to Charitable Foreign Missions

Drugs dispensed to Medicaid Patients from Street Brokers

Stolen Drugs

Legitimate Purchases

Samples

Secondary and Gray Market Drug Wholesalers

Foreign Drugs Repackaged for Sale to Nursing Homes and Pharmacies

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Counterfeit LIPITOR Repackaged for sale to Nursing Homes and Pharmacies.

Repackaging Hides Lot Number and Original Packaging.

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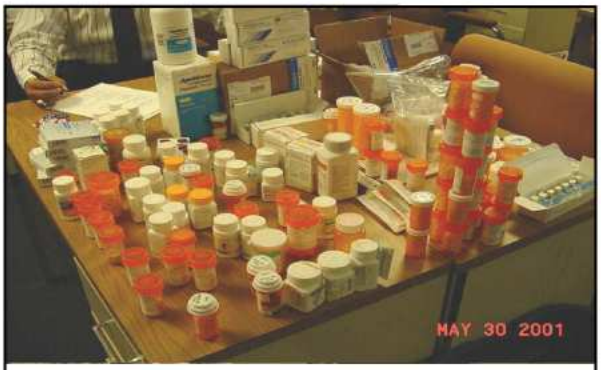

Dispensed Medicaid medications seized by City of Miami PD from a person dealing in Oxycontin. This "street broker" sells to others who then sell the product to Florida wholesalers.

Goo Gone, Lighter fluid and heat gun used to remove dispensing label from medications.

New Felony – Removing Rx Label with intent to further distribute

Drugs previously dispensed to patients. Label damaged by solvents used to remove pharmacy label.

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Previously Dispensed HIV drugs. Cleaned o

Sorted by brand

Found in the trunk of a car.

Pedigree

1. **Big Three Wholesaler**
2. **Broward Wholesaler**
3. **Missouri Wholesaler**
4. **California Wholesaler**
5. **AZ Pharmacy**

Trizavir – 10 boxes purchased by AZ pharmacy. One bottle contained dispensing label of Pharmacy in Ft. Lauderdale.

11,000 boxes(10 vials each) Epogen 2,000 units traced to South Florida Pharmacy

Enough Epogen 2000 units to create the equivalent of 110,000 vials of Counterfeit Procrit 40,000 units 4 x 1ml

Potential of 5,000 patients treated for 5 months with 5% of prescribed dose.

Counterfeits

Expensive , Clear Liquids

- **Weaker Strength relabeled to Higher Strength**
- **Different Drug**
- **Saline or Water, Pathogens**

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Hijacked Trailers of Rx Drugs

INTENDED FOR EXPORT

Immune Globulin – 50 pallets Approx. $7,000,000 stored in unlicensed Florida warehouse. Sold for export, shipped to a freight forwarder, transferred to unlicensed warehouse. Being sold since first of year to Florida wholesalers. (One is AD for this brand)

The Prescription Drug Pedigree Challenge

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Florida Rx Drug Wholesale Definitions

- **499.012 Wholesale distribution; definitions; permits; applications; general requirements.**-
  (1) As used in this section, the term:
  (a) "Wholesale distribution" means distribution of prescription drugs to persons other than a consumer or patient
  (b) "Wholesale distributor" means any person engaged in wholesale distribution of prescription drugs in or into this state, including, but not limited to, manufacturers; repackers; own-label distributors; jobbers; private-label distributors; brokers; warehouses, including manufacturers' and distributors' warehouses, chain drug warehouses, and wholesale drug warehouses; independent wholesale drug traders; exporters; retail pharmacies; and the agents thereof that conduct wholesale distributions.

Florida Rx Drug Wholesale Definition

- 499.003 (15) "Distribute or distribution" means to sell; offer to sell; give away; transfer, whether by passage of title, physical movement, or both; deliver; or offer to deliver. The term does not mean to administer or dispense.

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WHAT IS A FLORIDA PEDIGREE?

- "DOCUMENT" recording each distribution of a given prescription (Rx) drug, from sale by a manufacturer … until final sale to a pharmacy or other person administering or dispensing the drug.
- Electronic v. Paper Pedigrees
- Both paper and electronic documents may be used to meet pedigree requirements.
- Both Paper and Electronic must comply with record retention requirements.

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Florida Rx Drug Wholesaler Pedigree Requirements

- Repackagers must provide pedigrees
- Pedigrees must be kept separate from other records
- Pedigree must be provided for every sale of Rx Drugs.
- Pedigrees must be retained for 3 years.
- All pedigrees must be authenticated back to the Manufacturer (By the Mfr)
- Chain Pharmacy Warehouses – no pedigree within chain

Florida Rx Drug Wholesaler Pedigree Requirements

- Pedigree is required for Drop Shipments
- Pedigree is required for Medical Device Kits/Trays that contain Rx Drugs.
- Returns must appear on Pedigree >7 days
- Brokers must be licensed and provide pedigrees

Florida Rx Drug Wholesale Licensing Restrictions

- 499.01(1) (c) Rx Drug Wholesaler can not be issued in same name of a person or establishment authorized to purchase Rx drugs in this state. A retail pharmacy drug wholesaler will be issued a permit in the name of its retail pharmacy permit.
- (d) A permit for a prescription drug manufacturer, prescription drug repackager, prescription drug wholesaler, or retail pharmacy wholesaler may not be issued to the address of a health care entity or to a pharmacy licensed under chapter 465

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MISC. FLA. REQUIREMENTS

- **SALES INVOICE MUST HAVE THE NAME AND STATE LICENSED NUMBER OF PERSON AUTHORIZED TO PURCHASE RX DRUGS.**
- **ANNUAL INVENTORY OF RX DRUGS**
- **MINIMUM # OF TRANSACTIONS TO RENEW**
- **$100,000 Bond**
- **Criminal Background Checks**
- **No grace period for Expired Licenses**

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Florida Pedigree

- **Criminal Penalties regarding Pedigree Papers in section 499.0051, F.S. Criminal acts involving contraband or adulterated drugs.--**
- (1) FAILURE TO MAINTAIN OR DELIVER PEDIGREE PAPERS.–
- (2) FAILURE TO AUTHENTICATE PEDIGREE PAPERS.–
- (3) FORGERY OF PEDIGREE PAPERS

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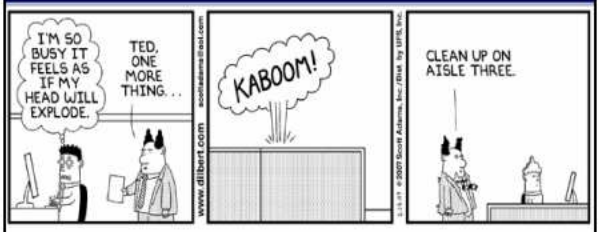
Contraband

"Contraband legend drug"
means any adulterated drug, as defined in s. 499.006, any counterfeit drug, as defined in this section, and also means any legend drug for which a pedigree paper does not exist, or for which the pedigree paper in existence has been forged, counterfeited, falsely created, or contains any altered, false, or misrepresented matter.

"Adulterated drug"
a legend drug for which the required pedigree paper is nonexistent, fraudulent, or incomplete under the requirements of ss. 499.001-499.081 or applicable rules, or that has been purchased, held, sold, or distributed at any time by a person not authorized under federal or state law to do so.

Pedigree Overload



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Direct Purchase Pedigree

- Amended full Pedigree law set to take effect July 1, 2006
- Requires statement for drugs that are purchased directly from the drug's manufacturer; "This wholesale distributor purchased the specific unit of the prescription drug directly from the manufacturer."
- A wholesale distributor must have purchased the specific unit of the drug directly from the manufacturer
- Must distribute the specific unit directly or through an intracompany transfer to a chain pharmacy warehouse or a person authorized by law to purchase prescription drugs for administering or dispensing. One intervening intra-company transfer allowed.

Pedigree Requirements - DPS

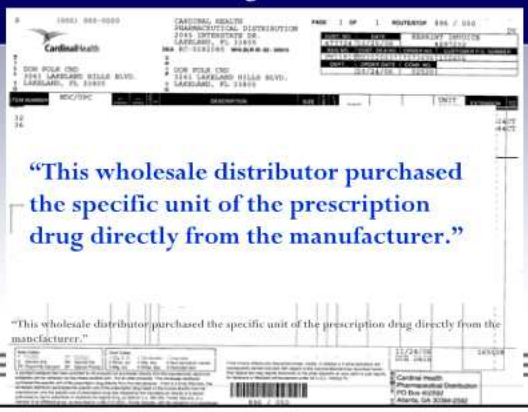
Direct Purchase Pedigree Requirements

- Must use the exact statement "This wholesale distributor purchased the specific unit of the prescription drug directly from the manufacturer." The statement pertains to the exact bottle being sold
- NDC # of the drug
- Name and address of seller
- Name and address of purchaser
- Name of the Drug as it appears on the label
- Strength, Dosage Form, and Quantity of the Drug

Wholesaler must maintain and make available upon request:

- the point of origin of the prescription drugs, including intracompany transfers;
- the date of the shipment from the manufacturer to the wholesale distributor;
- the lot numbers of such drugs; and
- the invoice numbers from the manufacturer.

Direct Purchase Pedigree – New 7/1/2006



Pharmacy Pedigree Requirements

- Insure receipt of a pedigree before placing drugs in stock. (Either Standard or Direct Purchase Pedigree)
- Maintain copies of all pedigree papers received. Same requirement as for invoices. 3 years
- Authentication is not required.
- Retail Pharmacy Wholesalers must provide pedigrees

Florida Pedigree AUTHENTICATION

- **499.003(4) "Authenticate" means to affirmatively verify before any distribution of a legend drug occurs that each transaction listed on the pedigree paper has occurred.**
- **Authentication is verifying each transaction reflected on the pedigree**

AUTHENTICATION of PEDIGREES

Methods to authenticate

1. **Receipt of invoice (shipping document)**
2. **Telephone call to seller (Signed Statement)**
3. **Email communication**
4. **Verification on web-based system**
5. **Receipt of unaltered copy of prior pedigrees**
6. **Self Authenticating Pedigree**
   - **Software using digital signatures**
   - **If Document sucessfully opens it indicates no changes have been made to all previous information on the pedigree**
7. **Written agreement with a Primary Wholesaler who agrees to purchase only from Mfr.**

Electronic Drug Pedigree Standard

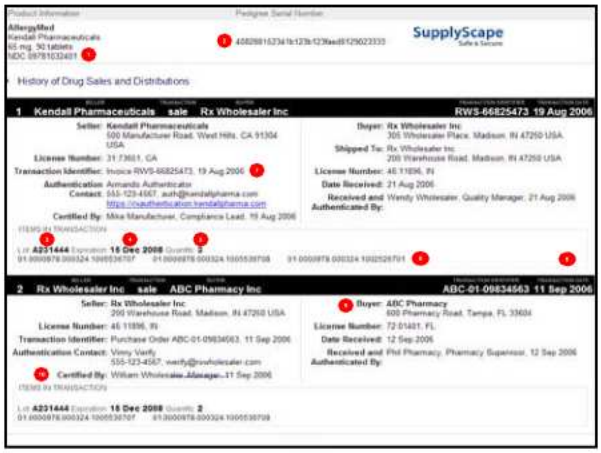
•Contains Several Hundred Pages of Standards

EPCglobal Inc Ratifies Electronic Pedigree Standard

Provides Platform for Compliance for Pedigree Laws Requiring a Document-Based Approach

BRUSSELS, Belgium – January 11, 2007 – GS1 EPCglobal, the not-for-profit standards organization dedicated to driving global adoption of the Electronic Product Code (EPC) for supply chain excellence, today announced the ratification of the Electronic Pedigree Document specification.

The new standard was developed to help companies that are serializing products using EPC technology to comply with pedigree regulations, such as ones recently enacted in multiple states within the United States. The initial focus of the EPCglobal Electronic Pedigree Document standard was the Florida Drug Pedigree Act, but it was designed to be usable as a platform to support a wide variety of pedigree process applications.



Standard Rx Drug Pedigree

Standard Prescription Drug Pedigree provided by Drug Wholesalers to customers (including pharmacies and practitioners).

Florida Pedigree Form (Wholesaler)

FLORIDA DEPARTMENT OF HEALTH

(Wholesaler's name)

PRESCRIPTION (LEGEND) DRUG PEDIGREE

History of Drug Sales and Distributions

Legend Drug Name, Strength, Dosage Form, Container Size:

☐ This is a repackaged drug (requires repackager's pedigree information and authentication of repackager's pedigree)

NDC (optional):

Lot Number	Quantity	Unique Serial #

Reference* Number:
Document Type:
Reference* Date:
(related to the sale by the wholesaler identified above)

OWNERSHIP HISTORY

PHYSICAL DISTRIBUTION HISTORY
(if different from the owner information)

Manufacturer's Name
Manufacturer's information for authentication:

1. *Wholesaler that purchased from the MANUFACTURER or a REPACKAGER (which requires authentication)*

Name:
Address:

Date Purchased & Ref * #
Print Name of Recipient:
Signature of Recipient:
Name of Authenticator:
Signature of Authenticator:
To authenticate a subsequent transaction, contact:
Name:
Telephone Number:
Email address:

Name:
Address:

Date Received & Ref * #
Print Name of Recipient:
Signature of Recipient:
Name of Authenticator:
Signature of Authenticator:
To authenticate a subsequent transaction, contact:
Name:
Telephone Number:
Email address:

Florida Pedigree Form (Wholesaler)

2. #1 Above SOLD TO:
Name:
Address:

SHIPPED TO:
Name:
Address:

Date Purchased & Ref * #
Print Name of Recipient:
Signature of Recipient:
Name of Authenticator:
Signature of Authenticator:
To authenticate a subsequent transaction, contact:
Name:
Telephone Number:
Email address:

Date Received & Ref * #
Print Name of Recipient:
Signature of Recipient:
Name of Authenticator:
Signature of Authenticator:
To authenticate a subsequent transaction, contact:
Name:
Telephone Number:
Email address:

3. #2 Above SOLD TO:
Name:
Address:

SHIPPED TO:
Name:
Address:

Date Purchased & Ref * #
Print Name of Recipient:
Signature of Recipient:
Name of Authenticator:
Signature of Authenticator:
To authenticate a subsequent transaction, contact:
Name:
Telephone Number:
Email address:

Date Received & Ref * #
Print Name of Recipient:
Signature of Recipient:
Name of Authenticator:
Signature of Authenticator:
To authenticate a subsequent transaction, contact:
Name:
Telephone Number:
Email address:

I swear or affirm that the information contained on this pedigree is accurate and complete and that prior sales and distributions have been authenticated, if required.

Signature (authorized to bind the company) Print Name and Title Date

Page ____ of ____ pages

* Reference Number should be identified as an invoice, purchase order, shipping document number or similar unique identifier.

The Safety of the U.S. Drug Supply is Improving

THE WALL STREET JOURNAL. ONLINE

May 6, 2005

HEALTH

Cardinal Health Ends Drug Trading

Move Is Regarded by Some As Step to Leave Business Blamed for Fake Products

By HEATHER WON TESORIERO
Staff Reporter of THE WALL STREET JOURNAL
May 6, 2005; Page B2

Drug wholesaler **Cardinal Health** Inc. will discontinue its pharmaceutical-trading business, which bought and sold drugs among secondary wholesalers, the company said.

Cardinal told employees of the change yesterday. A spokesman said the Dublin, Ohio, company's decision to discontinue the pharmaceutical-trading operations was "a business decision" motivated by shifts within the industry.

But some observers felt the move was an effort to exit from a business blamed for allowing counterfeit drugs to reach consumers.

Amerisource Bergen

Mckesson

Florida Wholesale Distributors

- 2002 – 475 instate, 975 out-of-state
- 2007 – 172 instate, 196 out-of-state

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Jim Dahl – Former FDA / OCI Deputy Director

Final FDA Counterfeit Drug Task Force 2/9/06

- **Primary Reasons for Opposing Pedigree Rules**
  - **The Drugs are Counterfeit or Obtained Illegally and Seller Cannot Risk Identifying their True Origin**
  - **Seller Does Not Want to Reveal Their Sources**
- **Unscrupulous Gray-Market Buyers**
  - **Plausible Deniability**
  - **"Don't Ask - Don't Tell"**
  - **Willful Blindness**

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Jim Dahl – Former FDA / OCI Deputy Director

Final FDA Counterfeit Drug Task Force 2/9/06

- **Wholesale Drug Diversion**
  - **Single Biggest Factor Contributing to Counterfeit Drugs in the Supply Chain**
  - **First in OCI Arrests**
  - **First in OCI Convictions**
  - **First in Number of OCI Cases**
  - **First in OCI Workhours**
- **Implement the Pedigree Regs**
- **Continue to Prosecute Those Who Do Not Provide Pedigrees**

Why do we have a Rx Drug Pedigree Law?

IN THE CIRCUIT COURT OF THE ELEVENTH JUDICIAL CIRCUIT, IN AND FOR MIAMI-DADE COUNTY, FLORIDA

STATE OF FLORIDA

vs. AFFIDAVIT IN SUPPORT OF ARREST WARRANT

DIEGO L. ESPIN

Your Affiant, KEMLY WOOD, is an agent for the Florida Department of Law Enforcement, and has been employed for the past 2 years. Prior to your Affiant's employment as an agent with the Florida Department of Law Enforcement, your Affiant was a Forensic drug chemist with the Florida Department of Law Enforcement.

Your Affiant alleges that there is probable cause to believe that the Defendant in the above-captioned case has committed the crime of FORGERY OF PRODUCTION OF LEGEND DRUG LABELS in violation of Florida Statute 499.0051(7) and states in support thereof as follows:

1. On April 6, 2006, your Affiant and Special Agent Gary Timmons participated in a "sting" operation and subsequent arrest of Jose Luis "Papito" Perez. Perez has since been charged in Miami-Dade County with Trafficking in Contraband Legend Drugs. Following the "sting" operation a search of a warehouse used by Perez was executed. Inside the warehouse investigators found approximately $500,000.00 in adulterated and misbranded pharmaceuticals, and counterfeit labels for Seroquel®, Zerit®, Crixivan®, Reyataz®, Truvada®, Combivir®, and Viramune®, all legend drugs. Also found in the warehouse were thousands of counterfeit outserts, the labeling information attached to bottles of pharmaceutical products that explain how to safely prescribe and use the medicines. The total of counterfeit labels and outserts found in the warehouse, if placed on containers of product would have totaled $8,000,000.00. Other items found in the illicit, secret warehouse were cleaning agents, (lighter fluid, alcohol, Goof Off) commonly utilized in the removal of pharmacy dispensing labels by unscrupulous persons involved in drug diversion. Also found were bags of Zyprexa®, an expensive psychotropic medication and bingo cards of various drugs that were in the process of being 'shucked' of the pills for repacking into manufacturers containers to appear as new. Several dies were found in the warehouse of the size and font that would be utilized in changing the expiration dates on boxes of medications.

PAPITO

Jose Luis "Papito" Perez.

Trafficking in Contraband Legend Drugs.

January 26, 2007

Printer Diego L. Espin owner of Spin Quality Printers in Miami

Charged with FORGERY OF RX DRUG LABELS – 1ST Degree Felony

Papito – Warehouse Search April 2006

Inside the warehouse investigators found approximately $500,000.00 in adulterated and misbranded pharmaceuticals, and counterfeit labels for Seroquel®, Zerit®, Crixivan®, Reyataz®, Truvada®, Combivir®, and Viramune®, all legend drugs. Also found in the warehouse were thousands of counterfeit outserts, the labeling information attached to bottles of pharmaceutical products that explain how to safely prescribe and use the medicines. The total of counterfeit labels and outserts found in the warehouse, if placed on containers of product would have totaled $8,000,000.00. Other items found in the illicit, secret warehouse were cleaning agents, (lighter fluid, alcohol, Goof Off) commonly utilized in the removal of pharmacy dispensing labels by unscrupulous persons involved in drug diversion. Also found were bags of Zyprexa®, an expensive psychotropic medication and bingo cards of various drugs that were in the process of being 'shucked' of the pills for repacking into manufacturers containers to appear as new. Several dies were found in the warehouse of the size and font that would be utilized in changing the expiration dates on boxes of medications.

Papito – Printer's Warehouse 12/13/2006

- Numerous template films used for the reproduction of Rx drug labels for Zepexa®, Combivir®, Risperdal®, Epivir®, Sustiva®, Viread®, Trizivir®, and Viracept®. All known to be illegally sold by "Papito"
- Bottles of Seroquel® and Combivir®, both legend drugs, that Espin said were brought to him by "Papito" along with the template films
- Admitted doing business with "Papito" for as many as 5 years

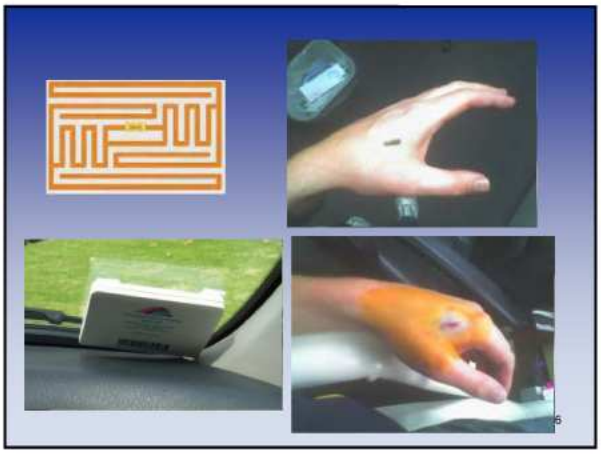
NABP Verified-Accredited Wholesale Distributors™ (VAWD™) Program

- **Based upon NABP Model Rules, State and Federal Laws**
- **Launched February 2005**
- **Pathway to Accreditation**
  - **Voluntary**
  - **State Regulation**
- **Application**
  - **Verification of licensure (Facility and Personnel)**
  - **Clearinghouse screening (Facility and Personnel)**
- **Policy and Procedure Evaluation**
- **Facility Inspection**
  - **Tour, staff interviews, documentation review**
  - **Periodic reviews and inspections**
- **Award Accreditation**

RFID – Radio Frequency Identification

RFID

- Radio Frequency Identification
- Electronic Track and Trace
- Each bottle (currently focused on cases, pallets) is Serialized with its own identifying number.
- Silicon tags, antennas, tag readers, and information systems.
- Additional benefits – inventory control, recalls, diversion, reduced dispensing errors.



RFID

- **Active RFID tags**
  - can be read at one hundred feet or more
  - needs battery power, which limits the lifetime
  - $20 or more each
  - physically larger than passive,may limit applications.
  - Battery outages can result in expensive misreads.
  - the capability to perform independent monitoring and control
  - the capability of initiating communications
  - the capability of performing diagnostics

MQA

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RFID

- **Passive RFID tags**
  - Only read at very short distances, a few feet. Greatly limits applications.
  - It may not be possible to include sensors that can use electricity for power.
  - Tag remains readable for a very long time, even after the product to which the tag is attached has been sold and is no longer being tracked.
  - Tag functions without a battery; Useful life of twenty years or more.
  - The tag is typically much less expensive to manufacture than active
  - Tag is much smaller (some tags are the size of a grain of rice) than active. Tags have almost unlimited applications in consumer goods and other areas.

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Counterfeit Medicines

- Although precise and detailed data on counterfeit medicines is difficult to obtain, estimates range from around 1% of sales in developed countries to over 10% in developing countries, depending on the geographical area. That range takes into consideration both regional disparities in the presence of counterfeits, and specific global market value shares. Apart from the huge differences between regions, variations can also be dramatic within countries, i.e. city versus rural areas, city versus city.
- WHO Fact sheet No 275 Revised 14 November 2006

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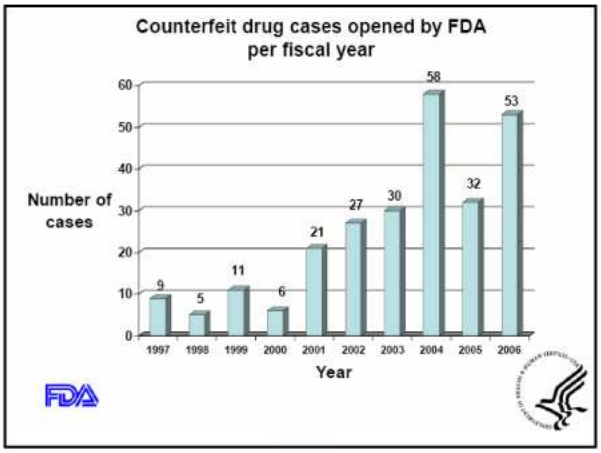

Counterfeit Medicines

- **The US based Centre for Medicines in the Public Interest predicts that counterfeit drug sales will reach US $75 billion globally in 2010, an increase of more than 90% from 2005.**

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Pedigree Challenges

- Virtual Companies
- Contract Manufacturer
- Contract Distributor
- Researchers IND sponsor approved drugs
- Analytical Labs
- Repackagers
- Reverse Distributors – Expired
- Reverse Logistics – Overstocks

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3PL

- A third-party logistics provider (abbreviated 3PL) is a firm that provides outsourced or "third party" logistics services to companies for part or sometimes all of their supply chain management function.
- Florida only allows for Manufacturers, not Wholesalers.
- Warehousing, picking, shipping, invoicing, accounts receivable, returns processing.

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3PLs – Drug Manufacturer

- the person is the holder of an approved New Drug Application (NDA), Abbreviated New Drug Application (ANDA), or New Animal Drug Application (NADA); or
- the person and establishment is a private label distributor and the private label distributor's prescription drugs are originally manufactured and labeled for the distributor and have not been repackaged; or
- the establishment is the distribution point for the manufacturer, contract manufacturer or private label distributor whether the establishment is a member of the manufacturer's affiliated group or is a contract distribution site;

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Virtual Manufacturer

- Owns rights to a Rx Drug (ANDA holder)
- Contract Manufacturer
- Contract Distributor (3PL)
- Passes title from a location in or outside Florida
- Location shipping and transferring title must be licensed.

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Reverse Logistics

- Company receives drugs from pharmacies of large chain such as excess stock and slow moving items.
- Drugs received from the chain pharmacies by the Reverse Logistics (RL) company inventoried and sent to other pharmacies in the chain that need the drugs.
- Chain will retain title. No title will pass to the RL company. Drugs sent to the RL company by the pharmacy could be from any source used by the Pharmacy. The RL company could be located in Florida or OOS.
- This is not occurring yet in FL, but is being done in other states.
- Q - What would the licensing and pedigree requirements be for this business arrangement/scenario?

Rx Medical Device Convenience Kits

- Florida considers the device manufacturer to also be a Rx Drug Repackager and therefore required to provide a Pedigree.
- In State repackagers must provide a pedigree
- Out-of-State repackagers licensed as – Out-of-State Rx Drug Wholesalers and are required to provide a pedigree for all wholesale distributions of Rx drugs.

Therasys System

+ INSTILLATION SPIKE

Therasys System

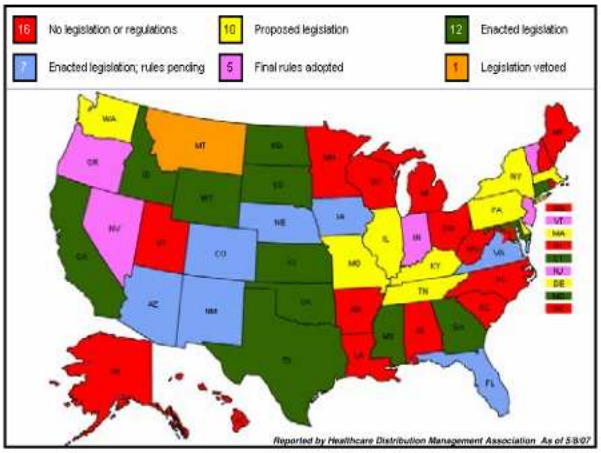
- One dose of TheraCys® consists of one 81 mg vial of reconstituted material further diluted in 50 mL sterile, preservative-free saline.
- Therasys – Sanofi sells vial, diluent, spike, + 50 cc NS
- Normal Saline from Hospira
- Sanofi Pasteur is wholesaler must pass pedigree

Investigational Drug Study Distributions

- Phase 4 – post approval studies
- No distribution exemption in Florida Law
- Research Hospital (Florida and Out of state, sponsors a study and receives drug from mfr. How to distribute to investigators.

EPC Global Electronic Pedigree Standard

- Standard applies California pedigree requirement that Manufacture initiate pedigree
- Florida allows first wholesaler to initiate pedigree



California

- 2004 Legislation passed
- 3/16/06 Announced implementation delayed 1/1/09?
- Requires Pedigree back to the manufacturer

Prescription Drug Protection

- 1987 - Goal
  - "We Only buy from licensed wholesalers."
- 2007
  - We only buy drugs directly from the Manufacturer; or
  - We only buy from licensed wholesalers; and
  - We conduct due diligence on our wholesale sources; and
  - We receive a document showing all previous sales of each unit of every prescription drug purchased; and
  - We authenticate each transaction of every drug purchased;

Thank You

Oh Well...I could be at the office.

Contact Information
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